

REMARKS/ARGUMENTS

With entry of this amendment, claims 1-13, 15, 18-19, 22-25, 27-37, 39-53 and 132-133 are pending, Claim 21 having been newly canceled. Claims 14-17, 20, 26, 38 and 54-131 were previously canceled. Claims 1-4, 15, 18, 22-25, 29-36 and 132-133 were examined on the merits. Claims 5-13, 19, 27-28, 37 and 39-53 stand withdrawn from further consideration.

Claims 1, 15, 24, 25, 132 and 133 are amended. Support for the amendments to claim 1 is found at, *e.g.*, page 30, line 1 to page 32, line 7, of the specification and in original Figure 5. Support for the amendments to Claims 15, 24, 25, 132 and 133 is set forth in the following remarks. No new matter is added by these amendments.

The specification has been amended to correct certain obvious typographical errors and to conform the specification to the figures as originally filed and to the second substitute sequence listing (discussed *infra*). The description of the SEQ ID NOS: 46 and 47 is amended to correspond to Figure 5 as originally filed and to the first substitute sequence listing. No new matter is added by these amendments.

Sequence Listing

Applicants request entry of a second amended sequence listing in adherence with 37 C.F.R. §§1.821 - 1.825. In order to comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, 37 C.F.R. §§ 1.821-1.825, Applicants submitted a sequence listing in paper and computer readable format (CRF) on July 10, 2001. Applicants later submitted a substitute sequence listing on January 10, 2003 which corrected the presentation of some sequences. The substitute sequence listing filed January 10, 2003 was resubmitted on February 11, 2003, in response to a telephonic request from the Examiner.

Upon further review, Applicants have noted that SEQ ID NOS:42, 45 and 47 of the sequence listing filed February 10, 2003 also contained typographical errors. This second substitute sequence listing, submitted herewith, properly presents SEQ ID NOS:42, 45 and 47.

These revisions conform the sequences of the sequence listing to the sequences presented in the specification and figures and thus do not constitute new matter.

This amendment is accompanied by a floppy disk containing the above named sequences, SEQ ID NOS:1-104, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk. The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy.

Objections

Specification

The Examiner objects to the description of Figure 5 at page 8. The description of Figure 5 has been amended to recite clarify that the polynucleotide region corresponding to the active enzyme portion set forth as amino acids 46-501 of SEQ ID NO:2 is set forth as SEQ ID NO: 42. Support for this amendment is found at *e.g.*, p. 10, lines 20-24 of the specification, and in Figure 5 as originally filed.

Claims

Claims 15, 23, 24 and 25 stand objected to as an allegedly improper quotation of the amino acid residues. As noted by the Examiner, the residues indicated in brackets correspond to residues of SEQ ID NO:2 and are set forth in SEQ ID NO:43. While Applicants submit Claims 15, 24 and 25, as written, clearly recite the indicated sequence, Claims 15, 24 and 25 are amended to delete the bracketed references to SEQ ID NO:2. The objection to Claim 23 is moot in view of the prior amendment of Claim 23. The additional objection to Claim 25, a typographical error, is also moot in view of the present amendment of that claim.

Rejections

35 U.S.C. § 112, Second Paragraph

Objection of Claims 18 and 27-36

The withdrawal of the prior rejection of Claims 18 and 27-36 is acknowledged.

Objection of Claims 2, 132 and 133

Claims 2, 132 and 133 stand rejected because they recite the limitation “the enzyme,” for which the Office Action alleges insufficient antecedent basis. Applicants respectfully disagree.

Claims 2, 132 and 133 depend from Claim 1. Claim 1 recites a β -secretase “enzyme protein.” Thus, Applicants submit Claim 1 provides antecedent basis for both “the enzyme” and “the protein.” Without acquiescing to the rejection, but to proceed with more compact prosecution, Claims 2, 132 and 133 are amended to recite “the protein.”

Claim 132 stands rejected as allegedly not further limiting Claim 1. This rejection is respectfully traversed. Initially, it is noted the Office Action misquotes the definition of “purified to apparent homogeneity” at page 18, lines 1-3 of the Specification. That definition recites: “A protein or polypeptide is generally considered to be ‘purified to apparent homogeneity’ if a sample containing it shows a single protein band on a silver-stained polyacrylamide electrophoretic gel.” Thus, a protein can be purified to apparent homogeneity as determined by, for example, non-denaturing gel electrophoresis or denaturing (*e.g.*, SDS) gel electrophoresis, and silver staining. Claim 132 therefore properly further limits Claim 1.

Claim 133 stands rejected as allegedly not further limiting Claim 1. This rejection is respectfully traversed. The purification of protein to apparent homogeneity refers to whether a single protein band is evident on a silver-stained polyacrylamide electrophoretic gel, and thus refers to the presence or absence of additional protein bands. A protein purified sufficiently to provide a suitable substrate for N-terminal amino acid determination indicates a type of purity reflecting the absence of substances that interfere with a protein sequencing reaction, and thus

can include removal of non-protein contaminants. Therefore, Claim 133 further limits Claim 1 by requiring a higher level of purity than required by Claim 1.

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. 112, Second Paragraph.

35 U.S.C. § 112, First Paragraph

Claims 1, 2-4, 22-24, 29-36 and 132-133 Stand Rejected Under 35 U.S.C. § 112, First Paragraph, for Allegedly Failing to Comply with the Written Description Requirement

Claims 1, 2-4, 22-24, 29-36 and 132-133 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Without acquiescing to the rejection, but to proceed with more compact prosecution of this case, Applicants amend Claim 1 to recite, *inter alia*, a protein purified to apparent homogeneity comprising a segment of a β -secretase enzyme protein comprising SEQ ID NO: 2, the segment comprising valine at a position corresponding to position 130 of SEQ ID NO: 2. (Applicants reserve the right to prosecute claims to the subject matter of original Claim 1 in a related application.)

Applicants respectfully submit Claim 1, as amended, complies with the written description requirement. Amended Claim 1 sets forth the structure of the claimed purified protein, as a segment of SEQ ID NO: 2, the segment comprising valine at a position corresponding to position 130 of SEQ ID NO: 2. Further, as acknowledged by the Examiner, the specification discloses numerous species of the recited β -secretase for which the structure is known, including SEQ ID NOS:43, 58, 67, 68, 69, 70, 71 and 75. Based on this disclosure, Applicants submit the specification provides sufficient description of the structure of the recited purified protein.

Applicants further submit the specification describes the structure/function relationship of proteins comprising the recited segments of SEQ ID NO: 2. Figures 5a-5e describe relationship between the primary sequence and functional regions of SEQ ID NO:2. Further, the specification describes active forms of β -secretase (*see* at pages 30-32). In addition,

the specification describes other functions of the recited β -secretase segments, such as, for example, the use of certain immunogenic fragments or oligopeptides of SEQ ID NO: 2 in screening therapeutic compounds in a variety of drug screening assays (*see* Specification, page 50, line 14 to page 51, line 21.)

Applicants therefore submit Claim 1 and dependent Claims 2-4, 22-24, 29-36 and 132-133 comply with the written description requirement.

Claims 1-4, 22-24, 26-36 and 132-133 Stand Rejected Under 35 U.S.C. § 112, First Paragraph, for Allegedly Failing to Comply with the Enablement Requirement

Claims 1-4, 22-24, 26-36 and 132-133 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Initially, Applicants note Claim 26 has been canceled and Claims 27-28 stand withdrawn. Applicants believe Claims 1-4, 22-24, 29-36 and 132-133 were intended and respond accordingly.

The Examiner alleges the claims encompass any purified protein comprising a segment of any β -secretase protein originating from any natural or man-made source, lacking a signal sequence and a putative proregion (collectively amino acids 1-45 of SEQ ID NO:2). Without acquiescing to the rejection, but to proceed with more compact prosecution of this case, Applicants amend Claim 1 to recite, *inter alia*, a segment of a β -secretase enzyme protein comprising SEQ ID NO:2, the segment comprising valine at a position corresponding to position 130 of SEQ ID NO:2. (Applicants reserve the right to prosecute claims to the subject matter of original claim 1 in a related application.)

Applicants submit amended Claim 1 is enabled such that a person of ordinary skill in the art can make and use the recited protein without undue experimentation. Claim 1, as amended, provides identifying characteristics of the claimed protein (*e.g.*, comprising a segment of a β -secretase enzyme protein comprising SEQ ID NO:2, the segment comprising valine at a position corresponding to position 130 of SEQ ID NO:2). Further, the specification describes the relationship between the primary structure and functional regions of SEQ ID NO: 2. (*See, e.g.*, Specification at pages 30-32 and Figures 5a-5e.) In addition, as acknowledged by the Examiner,

the instant specification provides examples of the recited genus of polypeptides, such as SEQ ID NOS:43, 58, 67, 68, 69 70, 71 and 75. The specification further describes a assays for determining whether a segment of β -secretase is active. (*See, e.g.*, Specification, at page 68, line 15 to page 71, line 32.) In addition, the specification also describes methods of selecting β -secretase inhibitor using, *inter alia*, isolated β -secretase, its ligand-binding, catalytic or immunogenic fragments or oligopeptides thereof. (*See, e.g.*, Specification, at page 50, line 14 to page 55, line 2.) Therefore, Applicants respectfully submit the specification properly enables Claims 1-4, 22-24, 29-36 and 132-133/

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 102

Rejections of Claims 18-20

The withdrawal of the prior rejections of Claims 18-20 is acknowledged.

Claims 1 and 22 Stand Rejected Under 35 U.S.C. § 102(e) as Allegedly Anticipated by Powell (U.S. 6,319,689)

Claims 1 and 22 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Powell (U.S. 6,319,689). This rejection is respectfully traversed.

Anticipation under § 102 requires that “each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.”

Verdegaal Bros. v. Union Oil Co. of Calif., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The “exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference.” *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 USPQ 409, 411 (Fed. Cir. 1984). *See also* MPEP 2131.

As explained in the response to the prior Office Action, Powell excludes at least one element that is set forth in Applicants’ Claims 1 and 22. Claims 1 and 22 are directed to a

protein comprising a segment of a β -secretase protein having a valine at a position corresponding to residue 130 of SEQ ID NO:2. Powell does not disclose such an amino acid sequence or a protein comprising a segment having the recited valine residue. Without acquiescing to the rejection, but to proceed with more compact prosecution of this case, Claim 1 is amended to further clarify the β -secretase enzyme protein comprises a segment of SEQ ID NO:2 comprising a valine at a position corresponding to valine 130 of the β -secretase enzyme protein of SEQ ID NO:2.

Applicants therefore respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102.

35 U.S.C. § 103

Rejections of Claims 24-25, 27-28 and 31-36

The withdrawal of the rejections of Claims 24-25, 27-28 and 31-36 is acknowledged.

Claims 23 and 29-30 Stand Rejected Under 35 U.S.C. § 103(a) as Allegedly Being Unpatentable Over Powell in View of the Common Knowledge in Molecular Biology

Claims 23 and 29-30 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Powell in view of the common knowledge in molecular biology. The rejection is respectfully traversed.

As discussed above, Powell fails to teach SEQ ID NO: 2. The combination of Powell further in view of the common knowledge in molecular biology does not establish a *prima facie* case of obviousness. Obviousness requires either that the “references must expressly or impliedly suggest the claimed combination or the Examiner must present a convincing line of reasoning as to why the invention would have been obvious in light of the teachings of the references.” *Ex Parte Clapp*, 227 USPQ 972, 973 (BPAI 1985). The Examiner must consider “all of the facts.” *In re Lunsford*, 148 USPQ 721, 725 (CCPA 1966). The Examiner is not free to “pick and choose” prior art that supports his position. *Akzo v. US International Trade Commission*, 1 USPQ2d at 1241, 1246 (Fed. Cir. 1986). Obviousness is not established where

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the prior art as a whole “gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.” *In re O'Farrell*, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

Without acquiescing to the rejection, but to proceed with more compact prosecution of this case, Claim 1 is amended to further clarify the protein comprises a segment of SEQ ID NO:2 having valine at a position corresponding to valine 130 of SEQ ID NO:2. The Powell reference does not expressly or impliedly suggest the invention of Claims 23 and 29-30. Claims 23 and 29-30 are directed to a crystalline composition of the protein of amended Claim 1. Applicants respectfully point out that the probability of success is 0% because Powell fails to teach SEQ ID NO: 2 of the present application. Based on the foregoing, it is respectfully submitted that the rejection should be withdrawn.

Applicants therefore respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103.

Non-Statutory and Statutory Double Patenting

Claims 1-4, 18, 22-25, 29-34, 36 and 132-133 Stand Provisionally Rejected for Alleged Obviousness-Type Double Patenting

Claims 1-4, 18, 22-25, 29-34, 36 and 132-133 stand provisionally rejected for obviousness type double patenting over certain claims of commonly owned U.S. Patent Application No. 09/724,569. Applicants propose these issues be held in abeyance until an indication of allowability in the present case. Applicants will then consider providing a terminal disclaimer over the cited case provided the cited case has been or is about to patented, the claims in the cited case have not been divided from those in the present case by restriction requirement or election of species, and the claims in the cited case are in conflict with those in the present case at this time.

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Claims 1-2 Stand Rejected for Alleged Obviousness-Type Double Patenting

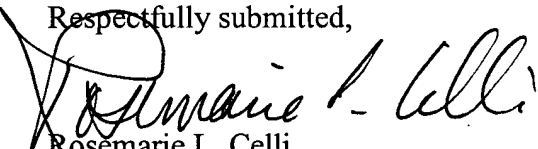
Claims 1 and 2 stand rejected for obviousness type double patenting over certain claims of commonly owned U.S. Patent No. 5,744,346. Applicants propose these issues be held in abeyance until an indication of allowability in the present case. Applicants will then consider providing a terminal disclaimer over the cited case, provided the claims in the cited case are in conflict with those in the present case at this time.

Claims 1-2 Stand Provisionally Rejected for Statutory Double Patenting

Claims 15 and 24 stand provisionally rejected for statutory double patenting over certain claims of commonly owned U.S. Patent Application No. 09/724,569. Applicants propose these issues be held in abeyance until an indication of allowability in the present case. Applicants will then consider providing a terminal disclaimer over the cited case provided the cited case has been or is about to patented, the claims in the cited case have not been divided from those in the present case by restriction requirement or election of species, and the claims in the cited case are in conflict with those in the present case at this time.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,


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